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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/798,037	03/11/2004	Jeffrey Robbins	CHM02-GN054	5033

30074 7590 03/21/2007

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EXAMINER	
CHEN, SHIN LIN	
ART UNIT	PAPER NUMBER
1632	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/21/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/798,037	ROBBINS, JEFFREY	
	Examiner	Art Unit	
	Shin-Lin Chen	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 January 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *10-18,35-39 and 50-52* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *10-18,35-39 and 50-52* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1-5-07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment filed 1-5-07 has been entered. Claims 37-39 have been amended. Claims 19-34 and 40-49 have been canceled. Claims 50-52 have been added. Claims 10-18, 35-39 and 50-52 are pending and under consideration.

Double Patenting

1. Applicant is advised that should claim 12 be found allowable, claim 16 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). Applicant indicates that upon allowance of claim 12, applicant will cancel claim 16 (amendment, p. 8).

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 10-18, 36 and 38 remain rejected and newly added claims 50-52 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention and is repeated for the reasons set forth in the preceding Official action mailed 10-6-06. Applicant's arguments filed 1-5-07 have been fully considered but they are not persuasive.

Applicant cites definition of "capable of" in Dictionary.com website as "having the ability or capacity for" (amendment, p. 9). This is not found persuasive because of the reasons set forth in the preceding Official action mailed 10-6-06. It is unclear as to the metes and bounds of what would be considered "capable of". It is unclear **to what extent of ability or capacity** is considered "capable of".

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 39 and 51 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant's amendment filed 1-5-07 necessitates this new ground of rejection.

The amended claim 39 and the newly added claim 51 recite "altered cardiac contractility", which is considered new subject matter. Applicant cites support for the phenotype of "altered cardiac contractility" throughout the specification and particularly in figures 2, 3, 5 and 6 and in paragraph 55 on page 20 and pages 40-42 (amendment, p. 10). However, paragraph 55 on page 20 only recites "contractility" but fails to mention "altered cardiac contractility". Pages 40-42 only discusses 5 transgenic rabbits survive increased pacing rates after surgical implantation of the pacemakers into those rabbits, and the shortening fraction of transgenic and

non-transgenic rabbits. Figure 2 discloses results of RNA analysis of cardiac tissue from transgenic and non-transgenic rabbits. Figure 3 shows transgenic rabbits have higher actin-activated ATPase activity than non-transgenic rabbits. Figure 5 shows transgenic rabbits have higher shortening fraction than non-transgenic rabbits. Figure 6 shows stress-velocity relationships of transgenic and non-transgenic rabbits. None of the provided evidence supports the phenotype of "altered cardiac contractility" of the claimed transgenic rabbits. The specification fails to provide sufficient support for the phrase set forth above. Thus, the phrase "altered cardiac contractility" in the amended claim 39 and the newly added claim 51 is considered new subject matter.

Claim Rejections - 35 USC § 101

6. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 10-18 and 35-39 remain rejected and newly added claims 50-52 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility and is repeated for the reasons set forth in the preceding Official action mailed 10-6-06. Applicant's arguments filed 1-5-07 have been fully considered but they are not persuasive.

Applicant argues that the transgenic rabbits of the invention exhibit an altered cardiopathic phenotype, such as an increased or decreased susceptibility to cardiopathy, therefore, the rabbits can be used in studying heart disease and conditions or to identify anti-cadiopathic compounds. Claim 37 and 38 have been amended to recite "exhibit an altered susceptibility to cardiopathy" and claim 39 has been amended to recite "altered cardiac contractility" phenotype of the claimed transgenic rabbits. Thus, the claimed transgenic rabbits have utility in studying heart disease and conditions (amendment, p. 9-11). This is not found persuasive because of the reasons set forth in the preceding Official action mailed 10-6-06. The specification fails to disclose any phenotype of the claimed transgenic animal or transgenic rabbit. As discussed above, the phrase "altered cardiac contractility" is considered new matter because the specification fails to provide sufficient support for such phrase. The phenotype of "altered susceptibility to cardiopathy" is only one of various phenotypes of interest in cardiac tissue (e.g. [0055]. The specification provides NO evidence for the phenotypes of "altered susceptibility to cardiopathy" and "altered cardiac contractility" of the claimed transgenic rabbits. It also appears that the state of the art shows that no phenotype has been observed in either transgenic rabbit or transgenic feline expressing wild-type human beta-MyHC. A transgenic rabbit having no phenotype is indistinguishable from a wild-type rabbit and does not have a specific and substantial utility or a well-established utility because one skilled in the art would not know where and what to look for in using said transgenic rabbit. Further, claims 10-18, 35 and 36 do not recite any phenotype of the claimed transgenic rabbits. Absent the phenotype of the claimed transgenic rabbit, no "real world" use of the claimed transgenic rabbit has been established. The specification also fails to provide a correlation between the altered

myosin isoform expression and any phenotype, if any, of the claimed transgenic rabbit or a correlation between the phenotype, if any, of the claimed transgenic rabbit and any disease or disorder, such as familial hypertrophic cardiomyopathies. No phenotype, such as a cardiopathic phenotype, has been disclosed for the claimed transgenic rabbit or transgenic animal. The asserted utility for the claimed transgenic rabbit or animal for studying heart disease and conditions, for studying familial hypertrophic cardiomyopathies or for identifying anti-cardiopathic compounds by monitoring cardiopathic phenotype of the transgenic rabbit does not appear to be specific and substantial because no phenotype has been disclosed for the claimed transgenic rabbit and no correlation between a phenotype, if any, and a particular disease or disorder has been established. Thus, claims 10-18 and 35-39 remain rejected and newly added claims 50-52 are rejected under 35 U.S.C. 101.

Claims 10-18 and 35-39 also remain rejected and newly added claims 50-52 are rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claim Rejections - 35 USC § 112

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 10-18 and 35-38 remain rejected and newly added claims 50-52 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description

requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention and is repeated for the reasons set forth in the preceding Official action mailed 10-6-06. Applicant's arguments filed 1-5-07 have been fully considered but they are not persuasive.

Applicant argues that claims 15 and 16 recite transgenic rabbits having the phenotype of altered expression of the heterologous nucleotide sequence, claims 37-38 and 50 recite transgenic rabbits having the phenotype of altered susceptibility to cardiopathy, claim 18 recited transgenic rabbits having the phenotype of altered myosin isoform expression, and claim 51 recites transgenic rabbits having the phenotype of altered cardiac contractility (amendment, p. 12). This is not found persuasive because of the reasons set forth in the preceding Official action mailed 10-6-06 and the reasons set forth above. The claims read on numerous transgenic rabbit expressing any heterologous polypeptide under the control of the promoter sequence of SEQ ID No. 1 or 2 or its variants, and transgenic rabbit expressing alpha or beta myosin heavy chain protein or its structural variants under the control of the promoter sequence of SEQ ID No. 1 or 2 or its variants. The claims encompass numerous transgenic rabbits having various unknown and unidentified phenotypes or having no phenotype. The specification fails to disclose any phenotype of the claimed transgenic rabbits. The phenotypes of various transgenic rabbits expressing any heterologous polypeptide, such as alpha or beta myosin heavy chain, under the control of the promoter sequence of SEQ ID No. 1 or 2 or its variants were unpredictable at the time of the invention. The structural features and phenotypes of the transgenic rabbits that can distinguish said transgenic rabbits from corresponding wild-type rabbits have not been disclosed.

The claims encompass transgenic rabbits expressing numerous different heterologous polypeptides under the control of the promoter sequence of SEQ ID No. 1 or 2 or its variants and the resulting phenotypes of said transgenic rabbits were unpredictable at the time of the invention. Therefore, it is apparent that applicant does not have possession of the claimed transgenic rabbits having the recited phenotype at the time of the filing and the written description requirement is not satisfied for the transgenic rabbits as claimed.

Applicant argues that transgenic rabbits comprising SEQ ID No. 2 operably linked to CAT reporter gene and transgenic rabbits expressing alpha-MHC under the control of beta-MHC promoter are generated (amendment, p. 13). This is not found persuasive because of the reasons set forth in the preceding Official action mailed 10-6-06 and the reasons set forth above. Although applicant may have possession of the transgenic rabbits disclosed in the specification, however, applicant does not have possession of the full scope of vast numbers of transgenic rabbits as claimed.

11. Claims 10-18 and 35-39 remain rejected and newly added claims 50-52 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention and is repeated for the reasons set forth in the preceding Official action mailed 10-6-06. Applicant's arguments filed 1-5-07 have been fully considered but they are not persuasive.

Applicant argues that the specification teaches the method of making the claimed transgenic rabbits and claims 15, 16, 18, 37-39 have been amended and the newly added claims

50-52 all recite phenotype of the transgenic rabbits, and reiterates the arguments regarding the recited phenotypes (amendment, p. 14). This is not found persuasive because of the reasons set forth in the preceding Official action mailed 10-6-06 and the reasons set forth above. It is noted that claims 15, 16 and 18 have NOT be amended. The claims read on numerous transgenic rabbits expressing any heterologous polypeptide under the control of the promoter sequence of SEQ ID No. 1 or 2 or its variants, and transgenic rabbit expressing alpha or beta myosin heavy chain protein or its structural variants under the control of the promoter sequence of SEQ ID No. 1 or 2 or its variants. The claims encompass numerous transgenic rabbits having various unknown and unidentified phenotypes or having no phenotype. The specification fails to provide a correlation between the altered myosin isoform expression and any phenotype, if any, of the claimed transgenic rabbit or a correlation between the phenotype, if any, of the claimed transgenic rabbit and any disease or disorder, such as familial hypertrophic cardiomyopathies. No phenotype, such as a cardiopathic phenotype, has been disclosed for the claimed transgenic rabbit. The art of transgenics at the time of the invention held that the resulting phenotype of a transgenic animal was unpredictable at the time of the invention. The individual gene of interest, promoter, enhancer, coding or non-coding sequences present in the transgene construct, the site of integration, etc., are all important factors that governs the expression of a transgene in a transgenic animal or rabbit. Further, the genetic background of the transgenic animal or rabbit has a large impact on the resulting phenotype of the transgenic animals or rabbit. In addition, it was known in the art the transcriptional activity of a promoter was unpredictable from mere the nucleotide sequence of a promoter. A slight change of a promoter sequence could result in dramatically increase or decrease in the transcriptional activity of said promoter. Variants of

promoter sequence SEQ ID No. 1 or 2 could also have dramatically different transcriptional activity as compared to the promoter sequence of SEQ ID No. 1 or 2. Biological function of a protein was unpredictable from mere amino acid sequence at the time of the invention. The unpredictable promoter activity of different promoter sequences and the unpredictable biological function of different proteins at the time of the invention add to the unpredictability of the resulting phenotype of the claimed transgenic animals and rabbits of the instant invention. Thus, one skilled in the art at the time of the invention would require undue experimentation to generate the full scope of the claimed transgenic rabbits, to determine the phenotypes of the claimed transgenic rabbits, and to determine how to use said transgenic rabbits.

Applicant cites Figures 5, 6 and example 8, and argues that the transgenic rabbits exhibit altered cardiac contractility (amendment, p. 14). This is not found persuasive because of the reasons set forth in the preceding Official action mailed 10-6-06 and the reasons set forth above. The phrase "altered cardiac contractility" is considered new matter as set forth above and it is unclear how the data in Figures 5, 6 and example 8 correlate to "altered cardiac contractility".

Applicant argues that claims 35, 37 and 39 only recite SEQ ID No. in the claim, and the other claims recite limitation of "being capable of initiating transcription in an animal cell" (amendment, p. 14). This is not found persuasive because of the reasons set forth in the preceding Official action mailed 10-6-06 and the reasons set forth above.

Conclusion

No claim is allowed.

12. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shin-Lin Chen whose telephone number is (571) 272-0726. The examiner can normally be reached on Monday to Friday from 9:30 am to 6 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on (571) 272-4517. The fax phone number for this group is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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Shin-Lin Chen, Ph.D.

SHIN-LIN CHEN
PRIMARY EXAMINER